REMARKS/ARGUMENTS

Claims 18-30 are pending and under consideration in the above-identified application.. Claims 19, 27 and 28 have been canceled without prejudice. Claims 18, 20 -26, 29 and 30 have been amended. No new matter has been added with each of the above amendments and support for each amendment is discussed herein below. Applicants respectfully request reconsideration of the pending claims in light of the above amendments and the below remarks.

Rejections under 35 U.S.C. § 102:

Claims 18, 19 and 22 have been rejected under 35 U.S.C. § 102(b) as being anticipated by US 5,338,686 (Hellerstein). In particular, the Examiner has alleged that Hellerstein teaches the method step as presented in claims 18, 19 and 22. As mentioned by Applicants and in Hellerstein, the Examiner notes that in both methods samples are taken from a biopolymer subunit pool. The Examiner has further noted that Applicants are arguing that the molar excess is calculated based on isotopomeric species, but again the Examiner does not see any difference between the method taught in Hellerstein and the instant application. In Hellerstein, the Examiner summarizes the method as including steps wherein samples are taken from a pool, the relative abundance of monoisotopic and isotopomeric peaks using mass spectrometry are measured, the difference between the peaks of the first and second samples are calculated, and the rate of biopolymer decay is determined. In addition, the Examiner alleges that even if isotopomer species are used, there is nothing in the instant claims to prevent the first sample of the biopolymer pool to encompass an isotopomer species. The Examiner concludes that the instant claims are broad, and that the method in Hellerstein reads on them.

In the interview conducted July 31, 2008 and subsequent interview held August 6, 2008 certain differences between the cited Hellerstein reference and present invention were discussed. In particular, Applicants noted that the present invention as claimed includes in steps c) and e) measuring the relative abundance of monoisotopic and isotopomeric peaks in the first (step c) and the second (step e) samples. The relative abundance in the claimed method includes

summing the peaks heights measured for all the monoisotopic and the isotopomeric peaks in each of steps c) and e). Hellerstein on the other hand states, for example at column 6, lines 64-68, "[a]s will be appreciated from the ensuing discussion, the isotopomers analyzed will contain at least one mass isotopically labeled subunit, and, for purposes of comparison, it is convenient to express the mass spectral peak heights as ratios". In addition, at column 7, lines 16-29, Hellerstein use instead of the monoisotopic and isotopomeric peaks, the isotopomer peak height ratio as expressed as a percentage total isotopomer content of the sample. As such the monoisotopic peak is not used in analyzing or calculating the molar excess. Each of these points were further discussed in Applicants' response after final rejection.

After further consultation with the Examiner's supervisor and another primary examiner, it was decided that the Hellerstein reference still applies for the following reasons. The Examiners allege that paragraph 27 defines monoisotopic mass as "a polymer or a fragment thereof as used herein defines the molecular weight of the polymer or of a fragment thereof in the absence of any naturally occurring stable isotope of the elements making up the polymer or a fragment thereof." In addition, the Examiners allege that "Monoisotopic peak" is not defined. Hellerstein is again alleged by the Examiners to calculate relative abundance using mass spectrometry and in Hellerstein the Examiner assert that the method uses the steps of taking samples from a pool, measuring the relative abundance of monoisotopic and isotopomeric peaks using mass spectrometry, calculating the differenced between the peaks of the first and second samples, and determining the rate of biopolymer decay. Further, the Examiners allege that although Applicants are arguing that the means of calculating the relative abundance are different, the Examiners do not believe that is clear from the claim language in the present invention that M zero is being used when measuring the relative abundance of monoisotopic and isotopomeric peaks. The Examiners believe that based on the claim language, Hellerstein and the present invention are both calculating relative abundance.

Applicants must again disagree with the interpretation of the claim language and the invention as set forth in the present application. The present invention as claimed includes in steps c) and e) measuring the relative abundance of monoisotopic and isotopomeric peaks in the

first (step c) and the second (step e) samples. The relative abundance in the claimed method includes summing the peaks heights measured for all the monoisotopic and the isotopomeric peaks in each of steps c) and e). Hellerstein on the other hand states, for example at column 6, lines 64-68, "[a]s will be appreciated from the ensuing discussion, the isotopomers analyzed will contain at least one mass isotopically labeled subunit, and, for purposes of comparison, it is convenient to express the mass spectral peak heights as ratios". In addition, at column 7, lines 16-29, Hellerstein use instead of the monoisotopic and isotopomeric peaks, the isotopomer peak height ratio as expressed as a percentage total isotopomer content of the sample. As such the monoisotopic peak is not used in analyzing or calculating the molar excess and although the general term "relative abundance" is used In both applications, the terms do not define the same quantitation.

Applicants also noted in the interview that Figures 3A through 3C of the present invention demonstrate why the monoisotopic peak, or M_0, is not used in the method of Hellerstein. In particular, the Figure 3 depicts data from the method of the present invention as used in calculating the rate of biopolymer synthesis, but calculating the rate of degradation would basically be the reverse. The monoisotopic peak, M_0, is the first peak in each of Figures 3A, 3B, and 3C. When stable isotope is included in the calculation the size of monoisotopic peak relative to the size of the isotopomeric peaks becomes smaller while the relative size of each isotopomeric peak becomes larger. With time, the relative size of the monoisotopic peak becomes smaller and the size of each isotopomeric peak becomes larger. As such, the effect of the increase, or decrease, in to amount of the monoisotopic peak is in the opposite direction as that of the isotopomeric peaks and this effect would alter the calculations of Hellerstein. Applicants believe that this aspect of the method are distinctly set forth in the claims. One of skill in the art would clearly understand the relationship between a monoisotopic peak and relative abundance as used in each application and in the present claims. Therefore, the claims as pending in the present application can not be considered so broad as to include the methods disclosed by Hellerstein.

Allowable Subject Matter

Claims 20, 21 and 23-30 remain objected as being dependent upon a rejected base claim, but are considered allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims. As discussed above, Applicants believe that in view of the above remarks the rejected base claims have been demonstrated to be unanticipated over the cited art and are allowable, Applicants in order to further expedite prosecution of certain subject matter disclosed and claim in the application have amended claims 18, 20-26, 29 and 30 to incorporate the allowed subject matter of claims 20, 21 and 23-30 and claims 19, 27, and 28 have been canceled without prejudice. In particular, claim 18 has been amended to recite "[a] method for determining the rate of degradation of a nucleic acid biopolymer". Claim 18 has been further amended for consistency to recite the nucleic acid biopolymer through all of the steps of the method. In addition, Claim 20 has been amended to depend from claim 18 instead of canceled claim 19. Still further, Claim 21 has been amended to recited "wherein the stable isotope-labeled monomer is a deoxynucleic acid, or a ribonucleic acid" to limit the monomer to those that make up a nucleic acid. Claims 22 through 26, 29 and 30 have been amended to be consistent with the subject matter the Examiner considers to be allowable. As such, Applicants believe that the pending claims are not anticipated by Hellerstein and the Examiner is respectfully requested to reconsider and withdraw the rejection of and/or objection to claims 18, 20-26, 29 and 30.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application,

please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 29 January 2009 By: Brian W. Poor
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